IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:		§		
		§		
	Amnon PELED et al.	§		
		§		
Serial No.:	10/649,873	§		
		§		
Filed:	August 28, 2003	§	Group Art Unit:	1646
		§		
For:	NOVEL CHEMOKINE BINDING PEPTIDES CAPABLE OF MODULATING THE BIOLOGICAL ACTIVITY OF CHEMOKINES	§		
		§	Attorney Docket:	**26732**
Examiner:	Hissong, Bruce D.	§		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF AMNON PELED AND ORLY EIZENBERG UNDER 37 CFR 1.132

I, Dr. Amnon Peled, presently serve as a CEO (Chief Executive Officer) of Biokine Therapeutics Ltd. I have founded Biokine Therapeutics Ltd. and have acted as the company's chief scientist from its inception. I also presently serve as a senior research fellow at the Gene Therapy Institute, Hadassah Medical Center, Jerusalem where I direct a laboratory, focusing on the role of chemokines and chemokine receptor based gene therapy for the treatment of cancer and immune diseases. I have a Ph.D. from the Department of Cell Biology at the Weizmann Institute of Science. I previously worked as a scientist at Millennium Pharmaceuticals Inc. in its Department of Inflammation. During my academic and professional carrier I have conducted and directed numerous research projects in the fields of chemokine-dependent gene

therapy and inflammation and have published more than 50 scientific publications in pear review journals.

I, Dr. Eizenberg, have acted as a vice president of Biokine Therapeutics Ltd. for Research and Development from its inception, at August 2000. I am an expert in the field of molecular biology, specifically in the area of oncogenes and tumor suppressor genes. I have a Ph.D. from the Weizmann Institute followed by post-doctoral studies in brain research and relative disorders, also from the Weizmann Institute. During my academic and professional carrier, I conducted and directed numerous research projects in the fields of virology, cancer and brain research and have published more than 15 scientific publications.

We are co-inventors of the subject matter claimed in the above-referenced U.S. Patent Application.

We have read the Examiner's Official Action dated November 1, 2006.

In the Official Action, the Examiner has stated, under the 35 U.S.C. 112, first paragraph enablement rejection, that the present invention does not reasonably providing enablement for methods of treating diseases by administering a peptidic chemokine modulator other than SEQ ID NO: 64 (BKT-P45). Specifically, the Examiner has stated that while the specification is enabling for a method of treating disease mediated by IL-8 by administering a therapeutically effective amount of the peptidic chemokine modulator BKT-45, it does not reasonably provide enablement for methods of treating disease by administering any other peptidic chemokine modulator. The Examiner has further stated that because many polypeptides can potentially comprise the recited amino acid residues, including two neighboring histidine residues, and have a positive charge, the breadth of the claims is excessive because the claims are drawn to methods of treating diseases by administering an unreasonably large number of potential peptides.

The Examiner has then concluded that a person of ordinary skill in the art would not be able to predict which of the many potential peptides/polypeptides could function as chemokine modulators and be effective in treating disease. Therefore, the

Examiner finds that it would require undue experimentation for one skilled in the art to make every possible peptide/polypeptide that meets the limitations of claim 10, and then use these peptides/polypeptides to modulate any chemokine, and ultimately treat disease.

As experts in the field of chemokine-dependent therapy, we contend that based of the data presented in the instant application, which delineates the experiments conducted so as to identify peptides that bind to chemokines and the common structural features thereof, and demonstrates the inhibitory effect of these peptides on certain chemokines, and the supportive data presented in Appendix A hereinbelow, which show additional results obtained for the binding and inhibitory activities of these peptides towards certain chemokines, any person skilled in the art would readily recognize that any peptide which features the unique structural characteristics of the claimed peptides (Family 2 peptides) is expected to exhibit the same binding and inhibition activities towards chemokines and hence would be able to practice the invention without undue experimentation.

The present invention is based on a process we have designed, in order to identify peptides that exhibit chemokine binding activity. To this end, two libraries, each containing more than 10^{11} peptides, were screened and only a fraction (about 200) of these peptides were found to bind chemokines. The structural features of some of the identified peptides were then analyzed and it has been surprisingly found that some of these peptides share common structural features. These peptides were divided into two main groups, according to these common structural features, denoted in the instant application as Family 1 and Family 2 peptides.

The fact that these peptides were found to have similar sequences is highly significant, and implies that these common features in the sequences of the peptides that bind chemokines are responsible for the binding activity of the peptides.

In order to further explore the activity of these peptides, their effect on the chemotactic activity of certain chemokines was tested. Some of the obtained data is presented in the Examples section of the instant application, and additional data is

presented in Appendix A that follows. These data concern the binding activity of 8 exemplary Family 2 peptides with respect to 5 tested chemokines.

These data clearly demonstrate that all of the tested Family 2 peptides bind at least one chemokine, that four of the eight tested Family 2 peptides bound most or all 5 chemokines tested, and that all 5 chemokines were bound by 3 to 6 of the eight tested family 2 peptides.

Thus, we have shown that the binding of chemokines is a general property of Family 2 peptides.

As is further presented in Appendix A, biovalidation studies demonstrate that Family 2 peptides that bind a chemokine also generally inhibit the activity of that chemokine. Both Family 2 peptides that were tested (BKT-P45 and BKT-P46) inhibit the activity of at least one chemokine, and chemokine activity was inhibited in 4 of the 5 cases tested.

Thus, we have shown that chemokines that are bound by Family 2 peptides are generally inhibited by these peptides, and that the ability to inhibit chemokine activity is a commonplace characteristic of Family 2 peptides.

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Serial No.: 10/649,873
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Group Art Unit: 1646
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We hereby further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application of any patent issuing thereon.

Prof. Amnon Peled

ביוקין תרפויטיקס בע"מ
BIOKIN THERAPEUTICS LTD

Prof. Orly Eizenberg

May 1, 2007.

Encl.:
Appendix A;
CV of Prof. Amnon Peled;
CV of Prof. Orly Eizenberg

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APPENDIX A

Chemokines:

Recombinant chemokines were ordered from PeproTech, Inc. (Rocky Hill, NJ, USA). Human SDF-1α (Cat. No. 300-28A), human MIG (Cat. No. 300-26) and human IL-8, (72 amino acids) (Cat. No. 200-08M), belong to the alpha-chemokine (C-X-C) family. Human MCP-1 (MCAF) (Cat. No. 300-04) and human eotaxin (Cat No. 300-21) belong to the beta-chemokine (C-C family). All chemokines were prepared according to the company recommendations.

Peptide synthesis:

Peptides were synthesized in the Weizmann Institute of Science, Rehovot, Israel, in order to perform tests for characterization of their influence on the biological activity of the chemokines. The format of the various synthesized peptides was as follows: The cyclic peptides, $ACX_7CGGGSK$-biotin-G and the linear peptides, $X_{12}GGGSK$-biotin-G. The peptides were biotinylated on their C-termini; the biotin will serve as a detector during the following experiments. Each synthetic peptide was dissolved to concentration of 1mg/ml (~0.6 mM) in 4% DMSO (Dimethyl Sulphoxide, Sigma, Cat. # D-2650).

ELISA analysis of the synthetic chemokine-binding peptide:

NUNC-Immuno maxisorp plates (Cat. No. 4-42404) were coated with the appropriate chemokine (0.1 ml/well, 0.1-1.0 μg/ml in 0.1 M $NaHCO_3$, pH 8.6), overnight at 4^0C. The plates were then blocked with 0.2 ml/well of blocking buffer (5mg/ml BSA in 0.1 $NaHCO_3$). Control wells were treated with blocking buffer alone, with no addition of target protein (chemokine). The plates were washed 6 times with PBST (0.1% Tween 20 in PBS), followed by incubation for 45 minutes at room temperature with 10-fold serial dilutions of individual synthetic peptides (10pg-10μg) with 1%BSA (PBST-BSA)/well. After the plates were washed 6 times with PBST, the bound peptides were probed by HRP-SA conjugate, diluted 1:10,000 to 1:20,000 in PBST-BSA, 0.1 ml/well for 45 minutes at room temperature. The target-bound

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synthetic peptides probed with HRP-SA were quantified by DAKO TMB one–step substrate system, followed by the addition of stop solution, HCl-H_2SO_4 mixture (0.1 ml/well) (1N HCl, 3N H_2SO_4). The results were analyzed by ELISA reader at OD_{450}.

T-Cell purification from fresh blood:

50ml blood was added to 10ml dextran (Dextran T-500 6% w/v) in PBS (phosphate buffer saline), and 7ml citrate buffer (25g citrate, 8g citric acid in 500ml PBS). The solution was incubated for 30 min at 25^{O} C. 10ml Ficoll 1077 (Sigma) was added to the bottom of the tube. The tube was then centrifuged at 2,000 rpm for 30 min, at 18^{O} C, (with the brake mode of the centrifuge off). The interphase was collected and washed twice with 8ml PBS-5% FCS (fetal calf serum), followed by centrifugation at 1,400 rpm, for 5 min, at 18^{O}C. The cells were re-suspended in PBS-5% FCS at a concentration less then 10^{8}/ml. 2ml of the cell solution were applied and incubated for 45 min at 25^{O} C on a Perspex Nylon wool column, which was pre-soaked with PBS-5% FCS. Each column was washed with 8ml PBS-5% FCS and the cells (T-cells and erythrocytes) were eluted by 50ml of 5mM EDTA in PBS. A red pellet was obtained by centrifugation at 1,400rpm, at 4^{O}C, for 5min, with the brake on. In order to perform lysis of the erythrocytes, the red pellet was re-suspended in 5ml lysis-buffer (155mM NH_4Cl, 10mM $KHCO_3$, 0.1mM EDTA, X0.1PBS) for 4 min, followed by immediate addition of 50ml of PBS-EDTA.

Following centrifugation at 1,400rpm, at 4^{O}C, for 5min with brake on, the pellet was washed again with 50ml PBS-EDTA and re-centrifuged under the same conditions. A white pellet was obtained and re-suspended in RPMI/10% FCS/L-glutamine/sodium pyruvate/antibiotics at a concentration of $3^{X}10^{6}$cells/ml. The cells were incubated for 2h at 37^{0}C, followed by collection of the non-adherent cells. The cells were ready for use in experiments after overnight incubation at 37^{0}C.

Preparation of adhesive substrates:

Human VCAM-1 (1μg/ml) and SDF-1α (intact or heat-inactivated) (2μg/ml) were dissolved in PBS buffered with 20mM bicarbonate, pH 8.5, and incubated on a

polystyrene plates overnight at 4 °C. The plates were then washed three times and blocked with human serum albumin (20mg/ml in PBS) for 2 h at 37°C.

Biovalidation:

Laminar flow assays were performed as follows. Polystyrene plates (B.D) were coated with soluble VCAM-1 at 10 μg/ml in the presence of 2 μg/ml HSA carrier. The plates were washed three times with PBS and blocked with HSA (20 μg/ml in PBS) for 2 hrs at room temperature. Alternatively, washed plates were coated with 10 μg/ml MIG chemokine in PBS for 30 min at room temperature, before being blocked with HSA. The plates were assembled as the lower wall of a parallel wall flow chamber and mounted on the stage of an inverted microscope. The peptide, as described previously, (10μg/ml) was allowed to settle on the substrate coated chamber wall for 10 min, at 37^0C and then washed. T cells ($5x10^6$/ml, purity >98%) were suspended in binding buffer, perfused into the chamber and allowed to settle on the substrate coated chamber wall for 1 min, at 37^0C. Flow was initiated and increased in 2 to 2.5 fold increments every 5 sec. generating controlled shear stresses on the wall. Cells were visualized in a 20x objective of an inverted phase-contrast Diaphot Microscope (Nikon, Japan) and photographed with a long integration LIS-700 CCD video camera (Applitech; Holon, Israel), connected to a video recorder (AG-6730 S-VHS, Panasonic, Japan). The number of adherent cells resisting detachment by the elevated shear forces was determined after each interval by analysis of videotaped cell images, and was expressed as the percent of originally settled cells. All adhesion experiments were performed at least three times on multiple test fields.

EXPERIMENTAL RESULTS

Binding assay:

Table 1 shows a summary of the binding activity of eight Family 2 peptides to 5 different chemokines, as tested by ELISA analysis. All chemokines tested were

bound by at least 3 of the 8 peptides tested, and MCP-1 was bound by 6 of the 8 peptides. In addition, several of the peptides bound more than one of the tested chemokines. BKT-P45 binds all five of the tested chemokines.

Table 1 – chemokine binding by family 2 compounds :

Peptide Name	Peptide Sequence	Bound Chemokine (at least)
BKT-P27	GDFNSGHHTTTR	MCP-1
BKT-P45	HHFHLPKLRPPV	IL-8, MCP1, MIG, SDF-1α, eotaxin
BKT-P55	HHTWDTRIWQAF	MCP-1
BKT-P46	LDYPIPQTVLHH	MCP-1, SDF-1α, eotaxin, MIG
BKT-P37	LLADTTHHRPWP	IL-8, MCP-1, MIG
BKT-P47	TRLVPSRYYHHP	MCP-1, SDF-1α, IL-8
BKT-P56	CHHNLSWEC	SDF-1α
BKT-P31	SFWHHHSPRSPL	eotaxin

Biovalidation:

Table 2 shows a summary of the biological activity results for two representative synthetic peptides belonging to family 2. Various chemokines were used in the biovalidation assay together with the adhesion receptor VCAM-1, in order to activate the adhesion of T cells in the system (as described in "Materials and Methods"). As an example, Figures 1a-c show the experimental results of the biovalidation assays for BKT-P46 with three different chemokines.

As can be seen in Table 2, both peptides checked showed an antagonistic effect towards more than one chemokine, although the degree of antagonism varies. Thus, BKT-P45 antagonizes the activity of both chemokines tested (IL-8 and MIG), whereas BKT-46 antagonizes the activity of MCP-1 and MIG, but not that of SDF-1α. In addition, the activity of MIG was reduced by both peptides by about 20 %, whereas the activities of the other chemokines (except for SDF-1α) were completely abolished.

Table 2 – biovalidation of family 2 compounds:

Peptide Name	**Peptide Sequence**	**Chemokine checked**	**Level of Antagonistic/Agonistic Effect**
BKT-P45	HHFHLPKLRPPV	IL-8	+++
		MIG	+
BKT-P46	LDYPIPQTVLHH	MIG	+
		MCP-1	+++
		SDF-1α	-

Legend: The percentage of antagonistic/agonistic effect is as follows:

+ 20%
++ 50%
+++ 100%
- No effect

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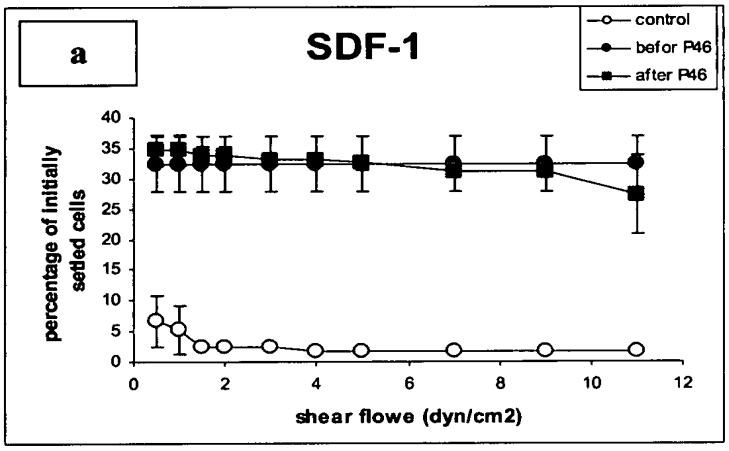
Figures 1(a-c) - biovalidation of compound BKT-P46



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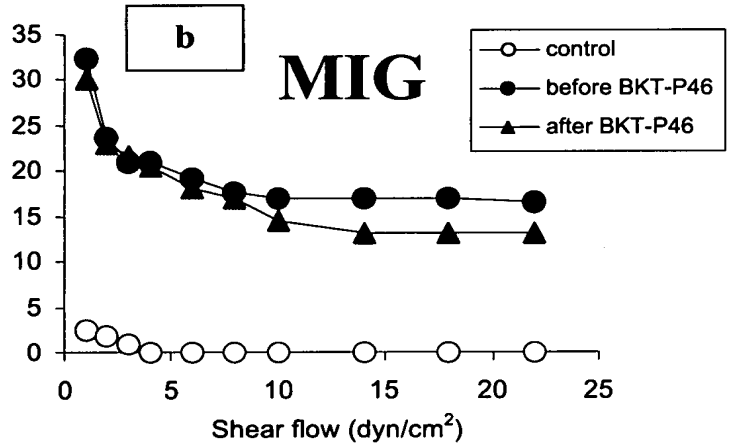

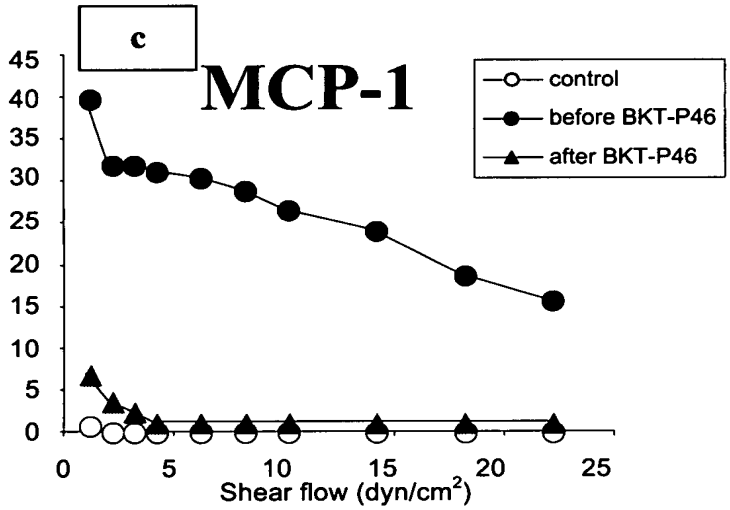

CURRICULUM VITAE

AMNON PELED, Ph.D.

A. Higher Education

1984 **B.Sc.** (cum laude) Hebrew University, Dept. of Plant Protection, Faculty of Agriculture, Rehovot, Israel

1987 **M.Sc.** Tel Aviv University School of Medicine, Dept. of Histology and Cell Biology under the guidance of Prof. A. Novogrodsky.

Thesis: "*Inhibition of Growth and Induction of Differentiation by Butyric Acid in Mouse and Human Melanoma Cell Lines*" (Refs. #1-2).

1994 **Ph.D.** The Weizmann Institute of Science, Dept. of Cell Biology, Rehovot, Israel, under the guidance of Prof. D. Zipori.

Thesis: "*Molecular and Cellular Analysis of Stroma Dependent Hemopoiesis*" (Refs. #3-8, 10, 13-14, 16-17).

1994-95 **Postdoctoral Fellow,** the Weizmann Institute of Science, Dept. of Cell Biology, Rehovot, Israel, under the guidance of Prof. V. Rotter.

Research Topic: "*The Effect of Wild Type and Alternative Spliced p53 on DNA Binding, Gene Activation, Apoptosis, Cell Cycle, and Differentiation of Myeloid Progenitors.*"

Dorot Fellow Award (Refs. # 9, 11-12, 15, 18, 20).

1995-97 **Postdoctoral Fellow,** Harvard Medical School, Dept. of Genetics, Boston, MA and Millenium Pharmaceuticals, Inc., Pharma-Division, under the guidance of Dr. J.C. Gutierrez-Ramos, Senior Director and Head of the Division of Immunology and Hematology, Boston, MA.

Research Topic: "*The Role of Chemokines, Chemokine Receptors in Inflammation and Hematopoiesis, Gene Discovery and Biological Validation of Novel and Known Chemokine Receptors and RGS Proteins, Potentially Involved in Controlling Allergic Inflammation. The Role of SDF-1/CXCR4 in Regulating Lung Allergic Inflammation.*" (Refs. # 19, 25).

1998-99 Postdoctoral Fellow, The Weizmann Institute of Science, Dept. of Immunology, Rehovot, Israel, under the guidance of Dr. Tsvee Lapidot.

Research Topic: *"The Role of CXCR4 and SDF-1 in Regulating the Homing and Engraftment of Human Hematopoietic Stem Cells"* (Refs. # 21-24, 26-29).

B. Appointments at the Hebrew University

4/2001- Principal Investigator, in the Department of Genetics and the Department of Microbiology. Member of the Goldyne Savad Institute of Gene Therapy, Hadassah University Hospital, Jerusalem, Israel.

Research Topic: *"Development of a Novel Chemokine/Chemokine-Receptor-based Therapeutic Approach for the Treatment of Cancer and Immune Diseases."*

4/2005- Assistant Professor, in the Department of Genetics and the Department of Microbiology. Member of the Goldyne Savad Institute of Gene Therapy, Hadassah University Hospital, Jerusalem, Israel.

C. Fellowships and Memberships

1995/6 Dorot Fellowship

1999- Member, the Israel Society of Immunology.

2000- Scientific Officer and founder of Biokine Therapeutics, Ltd.

2001- Member, Hadasit Scientific Advisory Board.

2002- Member, the Israel Society of Gene Therapy.

2007- Member, the Israel Society of stem cells

List of Publications

Doctoral Dissertation:

1995 The Weizmann Institute of Science, Dept. of Cell Biology, Rehovot, Israel, under the guidance of Prof. D. Zipori. Thesis: *"Molecular and Cellular Analysis of Stroma Dependent Hemopoiesis"*. (Refs. #3-8, 10, 13-14, 16-17).

Articles:

1. Nordenberg J., Peled A., Adler A., Novogrodsky A (1986). Inhibition of growth of human melanoma cells and enhancement of alkaline phosphatase activity by butyric acid. *Harefuah* (Hebrew) 111:21-23.

2. Nordenberg J., Wasserman L., Peled A., Malik Z., Stenzel KH., Novogrodsky A (1987). Biochemical and ultrastructural alterations accompany the anti proliferative effect of butyrate on melanoma cells. *Br. J. Cancer* 55:493-497.

3. Peled A., Zipori D., Abramsky O., Ovadia H., Shezen E (1991). Expression of □-smooth muscle actin in murine bone marrow stromal cells. *Blood* 78:304-309.

4. Peled A., Kalai M., Toledo J., Zipori D (1991). Stroma-cell dependent hematopoiesis. *Sem. Hematol.* 28:132-137.

5. Peled A., Zipori D (1992). A comparative study of growth stimulating and inhibiting activities secreted by a series of stromal cell lines. *Molecular Biology of Hemopoiesis* 2:247.

6. Gothelf Y., Peled A., Brosh N., Honigwachs- Shaanani J., Lee BC., Sternberg D., Carmi P., Levy A., Toledo J., Zipori D (1993). The restrictive role of stromal factors in hemopoiesis. *Negative Regulators of Hemopoiesis* 2:229-243.

7. Irlin Y., Peled A (1992). Thy-1 antigen-mediated adhesion of mouse lymphoid cells to stromal cells of haemopoetic origin. *Immunol. Letters* 33:233-237.

8. Benayahu D., Peled A., Zipori D (1994). Myeloblastic cell line expresses osteoclastic properties following coculture with marrow stromal adipocyte. *J. Cell. Biochem.* 56:374-384.

9. Wolkowicz R., Peled A., Elkind NB., Rotter V (1995). Augmented DNA-binding of p53 protein encoded by a carboxyl-terminal alternatively spliced mRNA is blocked by

p53 protein encoded by the regularly spliced form. *Proc. Nat. Acad. Sci.* (USA) 92:6842-6846. (Citation Index 10.27, Ranking 3/46, Number of Citations 30).

10. Peled A., Lee BC., Sternberg D., Toledo J., Aracil M., and Zipori D (1996). Interactions between leukemia cells and bone marrow stromal cells: Stroma-supported growth vs. serum dependence and the roles of TGF□and M-CSF. *Exp. Hematol.* 24:728-737. (4.012, 11/62, 10).

11. Peled A., Zipori D., Rotter V (1996). Cooperation between p53-dependent and p53 independent apoptotic pathways in myeloid cells. *Cancer Res.* 56:2148-2156. (8.649, 7/120, 46).

12. Peled A, Dov S., Elkind B., Wolkowicz R., Runzhao L., Rotter V (1996). The role of p53 in the induction of polyploidity of myelomonocytic leukemic M1/2 cells. *Oncogene* 13:1677-1685. (6.495, 12/120, 16).

13. Lee BC., Shav-Tal Y., Peled A., Gothelf Y., Jiang W., Toledo J., Ploemacher R., Haran-Ghera N., Zipori D (1996). A hematopoietic organ specific 49-kD nuclear antigen: Predominance in immature normal and tumor granulocytes and detection in hemopoietic precursor cells. *Blood* 87:2283-2291. (10.12, 2/62, 4).

14. Sternberg D., Peled A., Shezen E., Abramsky O., Toledo J., Meiver I., Bertolero F., Zipori D (1996). The effect of basic fibroblast growth factor on cloned murine bone marrow stromal cells. *Cytokines and Molecular Therapy* 2:29-38. (1.709, 29/124, 10).

15. Almog N., Li R., Peled A., Schwartz D., Wolkowicz R., Golfinger N., Pei H., Rotter V (1997). The murine C' terminal alternatively spliced p53 form induces an attenuated apoptosis in myeloid cells. *Mol. Cell. Biol.* 17:713-722. (8,142 18/156, 19).

16. Carramolino L., Lee BC., Zaballos A., Peled A., Barthelemy I., Shav-Tal Y., Prieto I., Carmi P., Gothelf Y., Buitrago G., Aracil M., Marquez G., Barbero JL., Zipori D (1997). SA-1, a nuclear protein encoded by one member of a novel gene family: detection in hemopoietic organs. *Gene* 195:151-159. (2.754, 46/120, 13).

17. Peled A., Shezen E., Schwartz D., Shav-Tal Y., Kushtai G., Lee BC., Zipori D. A novel monoclonal antibody recognizing a nuclear antigen expressed by proliferating cells. *Hybridoma* 16:325-334, 1997. (0.509, 109/114, 1).

18. Schwartz D., Almog N., Peled A., Goldfinger N., Rotter V (1997). Role of wild type p53 in the G2 phase: Regulation of the □-irradiation-induced delay and DNA repair". *Oncogene* 20:2597-2607. (6.495, 12/120, 56).

19. Peled A., Gonzalo JA., Lloyd C., Gutierrez-Ramos JC (1998). The Chemotactic Cytokine Eotaxin acts as a granulocyte-macrophage colony stimulating factor during lung inflammation. *Blood* 91:1909-1916. (10.12, 2/62, 30).

20. Wolkowicz R., Peled A., Elkind NB., Rotter V (1998). DNA-binding activity of wild-type p53 protein is mediated by the central part of the molecule and controlled by its C terminus. *Cancer Detect. Prev.* 22:1-13. (1.18, 95/120, 1).

21. Peled A., Petit I., Kollet O., Magid M., Ponomaryov T., Byk T., Nagler A., Ben-Hur H., Many A., Schultz L., Lider O., Alon R., Zipori D., Lapidot T (1999). Dependence of human stem cell engraftment and repopulation of NOD/SCID Mice on CXCR4. *Science* 283:845-848. (29.781; 2/46; 437; 429).

22. Peled A., Grabovsky V., Habler L, Sandbank J, Aranzena-Seisdedos F, Petit I., Ben-Hur H., Lapidot T.,and Alon R (1999). The Chemokine SDF-1 stimulates integrin-mediated arrest of $CD34^+$ cells on vascular endothelium under shear flow. *J. Clin. Invest.* 104, 1199-1211. (14.307; 3/72; 161; 153).

23. Kollet O, Peled A, Byk T, Ben-Hur H, Greiner D, Shultz L, and Lapidot T (2000). β2 Microglobulin deficient ($B2m^{null}$) NOD/SCID Mice are excellent recipients for studying human stem cell function. *Blood* 95:3102-3105. (10.12; 2/62; 42;40).

24. Peled A., Kollet O., Ponomaryov T., Petit I, Franitza S., Grabovsky V., Slav MM, Nagler A., Lider O, Alon A., Zipori D., Lapidot T (2000). The chemokine SDF-1 activates the integrins LFA-1, VLA-4 and VLA-5 on immature human $CD34^+$ cells: role in transendothelial/stromal migration and engraftment of NOD/SCID Mice. *Blood* 95:3289-3296. (10.12; 2/62; 172;161).

25. Gonzalo JA., Lloyd CM., Peled A., Delaney T, Coyle AJ., Gutierrez-Ramos JC (2000). Critical involvement of the chemotactic axis CXCR4/stromal cell-derived factor 1-□ in the inflammatory component of allergic airway disease. *J. Immunol.* 165:499-508. (6.702, 11/114, 44;43).

26. Grabovsky, V., Bleijs DA, Peled A, Cinamon G, Baleux F, Aranzena-Seisdedos F, Lapidot T, van Kooyk Y, Lobb RR, and Alon R (2000). Subsecond induction of alpha4 integrin clustering by immobilized chemokines stimulates leukocyte tethering and rolling on endothelial vascular cell adhesion molecule under flow conditions. *J. Exp. Med.* 192:1-12. (15.302, 2/72, 81;80).

27. Ponomaryov T, Peled A, Petit I, Taichman R, Habler L, Sandbank J, Arenzana-Seisdedos F, Magerus A, Caruz A, Fujii N, Nagler A, Lahav M, Szyper-Kravitz M, Zipori D, Lapidot T (2001). Induction of the chemokine stromal-derived factor-1 following DNA damage improves human stem cell function. *J. Clin. Invest.* 106:1331-1339, 2000. (14.307, 3/72, 67;59).

28. Kollet O, Spiegel A, Peled A, Petit I, Byk T, Hershkoviz R, Guetta E, Barkai G, Nagler A, and Lapidot T (2001). Rapid and efficient homing of human CD34(+)CD38(-/low)CXCR4(+) stem and progenitor cells to the bone marrow and spleen of NOD/SCID and NOD/SCID/B2m(null) mice. *Blood* 97:3283-91. (10.12, 2/62, 65;60)

29. Penido C, Castro-Faria-Neto HC, Vieira-de-Abreu A, Figueiredo RT, Peled A, Martins MA, Jose PJ, Williams TJ, and Bozza PT (2001). LPS induces eosinophil migration via CCR3 signaling through a mechanism independent of RANTES and Eotaxin. *Am. J. Respir. Cell Biol.* 25:707-16. (4.015, 42/156, 8;8)

30. Peled A [PI], Hardan I [C], Trakhtenbrot L [T], Gur E [C], Magid M [S], Darash-Yahana M [S], Cohen N [S], Grabovsky, V [C], Franitza S [S], Kollet O [T], Lider O [C], Alon R [C], Rechavi G [C], and Lapidot T [C] (2002). Immature leukemic $CD34^+CXCR4^+$ Cells from CML patients have reduced integrin-dependent migration and adhesion in response to the chemokine SDF-1. *Stem Cells* 20:259-266. (corresponding author) (5.802, 5/76, 13;13).

31. Kollet O [S], Petit I [S], Kahn J [S], Samira S [S], Dar A [S], Peled A [C], Deutsch V [C], Gunetti M [C], Piacibello W [C], Nagler A [C], and Lapidot T [PI] (2002). Human $CD34^+CXCR4^-$ sorted cells harbor intracellular CXCR4, which can functionally be expressed and provide NOD/SCID repopulation. *Blood* 100:2778-86. (10.12, 2/62, 28;26)

32. Petit I [S], Szyper-Kravitz M [C], Nagler A [C], Lahav M [C], Peled A [C], Habler L [S], Ponomaryov T [S], Taichman RS [C], Arenzana-Seisdedos F [C], Fujii N [C], Sandbank J [C], Zipori D [C], Lapidot T [PI] (2002). G-CSF induces stem cell mobilization by decreasing bone

marrow SDF-1 and up-regulating CXCR4. *Nat Immunol* 3:687-94. (28.180, 2/114, 80;77).

33. Beider K [S], Nagler A [C], Wald O [S], Franitza S [S], Dagan-Berger M [S], Wald H [C], Giladi H [C], Brocke S [C], Hanna J, Mandelboim O [C], Darash-Yahana M [S], Galun [C], Peled A [PI] (2003). Involvement of CXCR4 and IL-2 in the homing and retention of human NK and NK T cells to the bone marrow and spleen of NOD/SCID mice. *Blood* 102:1951-1958. (corresponding author) (10.12, 2/62, 11;4)

34. Hanna J [S]., Wald O [S], Goldman-Whol D [S], Prus D [S], Markel G [S], Gazit R [S], Katz G [S], Haimov-Kochman R [C], Fujii N [C], Yagel S [C], Peled A [C], Mandelboim O [PI] (2003). CXCL12 expression by invasive trophoblasts induces the specific migration of CD16- human natural killer cells. *Blood* 102:1569-1577. (10.12, 2/62, 9;8), equal contribution of Wald O a MD/Ph.D student in my laboratory.

35. Spiegel A [S], Kollet O [T], Peled A [C], Abel L [S], Nagler A [C], Bielorai B [C], Vormoor J [C], Fujii N [C], Rechavi G [C], and Lapidot T [PI] (2004). Unique SDF-1 induced activation of human precursor-B ALL cells due to altered CXCR4 signaling and expression. *Blood* 15:2900-2907. (10.12, 2/62, 2;2).

36. Avigdor A [S], Goichberg P [S], Shivtiel S [S], Dar A [S], Peled A [C], Samira S [S], Kollet O [T], Hershkoviz R [C], Alon R [C], Hardan I [C], Ben-Hur H [C], Naor D [C], Nagler A [C], and Lapidot T [PI] (2004). CD44 and hyaluronic acid cooperate with SDF-1 in the trafficking of human $CD34^+$ progenitors to the bone marrow. *Blood*. 15; 103:2981-2989. (10.12, 2/62, 2;2).

37. Wald O [S], Pappo O [C], Safadi R [C], Dagan-Berger M [S], Beider K [S], Wald H [C], Franitza S [S], Weiss I [S], Avniel S [S], Boaz P [S], Hanna J [S], Zamir G [C], Eid A [C], Mandelboim O [C], Spengler U [C], Galun E [C], and Peled A [PI] (2004). Involvement of the CXCL12/CXCR4 Pathway in Advanced Hepatitis C and B Virus-Associated Liver Disease. *Eur J Immunol*. , 34:1164-1174. (Corresponding author) (5.02, 17/114, 2;1).

38. Franitza S [S], Grabovsky V [C], Wald O, Weis I [S], Beider K [S], Dagan M [S], Darash-Yahana M [S], Nagler A [C], Brocke S [C], Galun E [C], Alon R [C], Peled A [PI] (2004). Differential usage of VLA-4 and CXCR4 by CD3+CD56+ NK T and CD56+CD16+ NK cells regulates their interaction with endothelial cells. *Eur J Immunol*,34:1333-1341. (corresponding author) (5.02, 17/114)

39. Darash-Yahana M [S], Pikarsky E [C], Karplus R [S], Boaz P [S], Zeira E [T], Abramovitch R [C], Galun E [C], and Peled A [PI] (2004). The Chemokine Receptor CXCR4 Stimulates Human Prostate tumor Growth and vascularization *In Vivo.* *FASEB* , 18:1240-1242., (corresponding author) (7.172, 22/156, 17;17).

40. Samira S [S], Ferrand C [S], Peled A [C], Nagler A [C], Ben-Hur H [C], Tovbin Y [C], Taylor N [C], Globerson A [C] and Lapidot T [PI] (2004). TNF□promotes extrathymic human T cell development in NOD/SCID mice. *Stem Cell,* 22:1085-1100 (5.802, 5/76).

41. Wald O [S], Pappo O [C], Ben Ari Z [C], Azzaria E [S], Gafnovitch I [C], Wald H [C], Weiss I [S], Hanna J [S], Galun E [C], and Peled A [PI] (2004). CCR5Δ32 allele reduces liver inflammation and liver damage in early stages of HCV infection. *EJIG* 31:249-252 (corresponding author). (1.009, 91/114).

42. Petit I, Spiegel A, Goichberg P, Peled A [C], Brodie C [C], Seger R [C], Nagler A [C], and Lapidot T [PI] (2004). Atypical PKC-zeta regulates SDF-1 induced chemotaxis of human $CD34^+$ stem cells. *JCI.* 115:168-176. (14.3, 3/72).

43. Byk T [S] Kahn J [S], Kollet O [T], Petit I [S], Samira S [S], Shivtiel S [S], Ben-Hur H [C], Peled A [C], Piacibello W [C] and Lapidot T [PI] (2004). Cycling G1 CD34+/CD38+ Cells Potentiate the Motility and Engraftment of Quiescent G0 CD34+/CD38-/low SCID Repopulating Cells. *Stem Cell*, 23:561-574. (5.802, 5/76).

44. Shani Avniel [S], Zaretski Arik [S], Alex maly [C], Assa Sagie [S], Hanna Ben Basst [C], Merav Darash Yahana [S], Ido D. Weiss [S], Boaz Pal [S], Ori Wald [S], Dean Ad-El [C], Nobutaka Fujii [C], Fernando Arenzana-Seisdedos [C], Steffen Jung [C], Eithan Galun [C], Eyal Gur [C] and Amnon Peled [PI]. Involvement of the CXCL12/CXCR4 pathway in the recovery of skin following burns JID, 126:468-476, 2006 (corresponding author). (4.238, 1/38).

45. Michal Dagan-Berger S, Rotem Feniger-Barish [S], Shani Avniel [S], Hanna Wald [C], Eithan Galun [C], Valentin Grabovsky [C], Ronen Alon [C], Arnon Nagler [C], Adit Ben-Baruch [C] and Amnon Peled [PI]. Role of CXCR3 carboxyl-terminus and third intracellular loop in receptor-mediated migration, adhesion and internalization in response to CXCL11. Blood, 15:3821-3831. 2006. (corresponding author), (10.12, 2/62).

46. Ori Wald [S], Ido Weiss [S], Hanna Wald [C], Lola Weiss [C], Yochay Bar-Shavit [S], Katia Beyder [S], Liat Flaishon [S], Arnon Nagler [C], Eithan Galun [C], Philip M. Murphy [C], Idit

Shachar [C], Joshua Farber [C], and Amnon Peled [PI]. IFN-□ acts on T cells to induce NK cell mobilization and accumulation in target organs. JI, 15:4716-4729, 2006 (corresponding author), (6.702, 11/114).

47. Golo Ahlenstiel, Agathe Iwan. Jacob Nattermann, Jürgen K. Rockstroh, Hans H. Brackmann, Bernd Kupfer, Olfert Landt, Amnon Peled [C], Tilman Sauerbruch, Ulrich Spengler and Rainer P. Woitas. Disease modifying effects of polymorphic RANTES gene alleles in HIV are abrogated by HCV confection. World J Gastroenterol. 2005 11:7631-7638.

48. Eldor R, Yeffet A, Baum K, Doviner V, Amar D, Ben-Neriah Y, Christofori G, Peled A [C], Carel JC, Boitard C, Klein T, Serup P, Eizirik DL, Melloul D. Conditional and specific NF-{kappa}B blockade protects pancreatic beta cells from diabetogenic agents. PNAS 2006.

49. Genetic Code Symmetry and an Efficient Algorithm for Efficient Cloning. Matan Gavish ,Amnon Peled, Benny Chor. In press, Bioinformatics, 2006. (5.742, 1/83).

50. Carlos Hidalgo-Grass, Inbal Mishalian, Mary Dan-Goor, Ilia Belotserkovsky, Yoni Eran, Victor Nizet, Amnon Peled and Emanuel Hanski. A streptococcal protease that locally degrades CXC chemokines subverting innate immune responses in the skin. In press, EMBO J. 2006.

51. Wald O, Izhar U, Amir G, Avniel S, Bar-Shavit Y, Wald H, Weiss I, Galun E and Peled A. CD4+,CXCR4high,CD69+,CD25+ tumor infiltrating T cells accumulate in NSCLC. In press JI 2006. (corresponding author). (6.702, 11/114)

[S=Student, C=Co investigator, T=Technician PI=Principal Investigator]

CURRICULUM VITAE OF Dr. ORLY EISENBERG

A. University Education and Additional Training

1977-1980	B.Sc. in Biology at Tel-Aviv University, Tel-Aviv, Israel.
1980-1983	M.Sc. in Virology at the Dept. of Virology, Weizmann Institute of Science, Rehovot, Israel. Title of thesis: "Biochemical Characterization of Canine-Distemper Virus". Supervision by: Prof. Shmuel Rozenblatt.
1983-1985	Research work in virology at the Dept. of Virology, Weizmann Institute of Science, Rehovot , Israel. Title of research: "Molecular Biology of Canine-Distemper Virus". With: Prof. Ernest Winocour.
1985-1991	Ph.D. in Oncogenes and Tumor Suppressor genes at the Dept. of Chemical Immunology, Weizmann Institute of Science, Rehovot, Israel. Title of thesis: "p53 as a possible gene expression modulator". Supervision: Prof. Moshe Oren.
1991-1994	Postdoctoral position at the Dept. of Neurobiology, Weizmann Institute of Science, Rehovot, Israel, with Prof. Michal Schwartz. Research subject: "Molecular Biology of Interleukin 2-like factor, associated with central nervous system regeneration".
2002	Course in "Establishment and Management of Start Up Companies". Mesila, Mati High Tech.

B. Positions Held and Academic Status

1994-1996	Research Scientist at the Dept. of Neurobiology, Weizmann Institute of Science, Rehovot, Israel.

1997-1998	Senior Scientist at the Israeli Institute for Biological Research, Ness-Ziona.
1998 to 2000	Senior Scientist at the ARO, The Volcani Center, Institute of Animal Science, Department of Poultry Science.
2000-to date	General Manager and VP R&D, Biokine Therapeutics Ltd, Science Park, Ness-Ziona.

D. Training Experience (including guidance of students and foreign scholars)

- Lecturer and running several lab courses at the Weizmann Institute of Science: "Virology" lab course, 1983; "Basic Tissue Culture Methods" lab course, 1984; "Methods in Molecular Biology" lab course, 1988.
- Working in Rockefeller University, New York, as a foreign scholar, for a month, in collaboration with the lab of Prof. Donald W. Pfaff, 1992.
- Guidance of several rotation's, master's and Ph.D students as well as Post-Doc's and M.D. students, through my entire academic route.

E. Editorial Responsibilities

1998	Reviewer of grant proposal for "The Israel Science Foundation".
2002	Evaluetor and reviwer in an Immunology grant comeettee of the "Israeli Ministry of Health ", Chief Scientist Office, Jerusalem, Israel.
2003	Evaluetor and reviwer in an Immunology grant comeettee of the "Israeli Ministry of Health ", Chief Scientist Office, Jerusalem, Israel.
2004	Evaluetor and reviwer in an Immunology grant comeettee of the "Israeli Ministry of Health ", Chief Scientist Office, Jerusalem, Israel.
2005	Evaluetor and reviwer in an Immunology grant comeettee of the "Israeli Ministry of Health ", Chief Scientist Office, Jerusalem, Israel.

2005 Evaluetor and reviwer in a Cancer grant comeettee of the "Israeli Ministry of Health ", Chief Scientist Office, Jerusalem, Israel.

2006 Evaluetor and reviwer in "Combating Cancer" grant comeettee, of the "European Commission's 6th Framework Programme for Research", Brussels, Belgium.

2006 Evaluetor and reviwer in an Immunology grant comeettee of the "Israeli Ministry of Health ", Chief Scientist Office, Jerusalem, Israel.

F. Research Grants

A. International Competitive Grants

1994 National Multiple Sclerosis Society grant. Title: "Involvement of p53 in demyelination", for one year.
Budget: $25,000/year. Researcher's part $ 25,000/year.

2005 FP6 Europian commission. Title: "Innovative Chemokine-based Therapeutic Strategies for Autoimmunity and Chronic Inflamation", for four years.
Budget: Euro 680,000

B. National Competitive Grants

1995 Ministry of Health, Chief Scientists Office grant. Title: "Involvement of p53 in demyelination: Implications for it's possible Involvement in Multiple Sclerosis", for one year.
Budget: $ 2,900/year. Researcher's part $ 2,900/year.

1999 Poultry Board Grant. Title: "Perosis in Broilers and Turkeys", for three years.
Budget: NIS 59,000/year. Researcher's part NIS 59,000/year.

2000 Ministry of Trade and Industry, Chief Scientist – Technological Incubators office. Title: " Development of Technology for Drug Development for Inflamatory Diseases", for two years/
Budget: $300,000, $150,000 per year.

2002 Ministry of Trade and Industry, Chief Scientist – Technological Incubators office. Title: "Development of Technologies for Identification of Drugs for Inflamatory Diseases", for one year.
Budget: $150,000.

2004 Ministry of Trade and Industry, Chief Scientist Office. Title: "Development of Technologies for Identification of Drugs for Inflamatory Diseases", for one year.
Budget: $530,000.

C. Other Research Grants

1995 Research fund by the head of the department of Neurobiology, The Weizmann Inst. of Science. Title: "Involvement of p53 in Apoptosis and Differentiation of Nerve Cells", for one year.
Budget: $ 31,000/year. Researcher's part $ 31,000/year.

1995 Research fund by the dean of the Biology Faculty, The Weizmann Inst. of Science. Title: "Involvement of p53 in Apoptotic death and Differentiation of Nerve Cells", for one year.
Budget: $23,500/year. Researcher's part $ 23,500/year.

D. Other investments in the Company.

2001 Private investment by several privat investors.
Budget: $200,000.

2003 Clal Biotechnology Industries Ltd Investments.
Budget: $1,100,000.

2005 European Company investment.
Budget: Euro 250,000.

2006 Private investment by several privat investors.
Budget: $130,000.

2007 Industrial and Private investor.
Budget: $525,000.

LIST OF PUBLICATIONS

1. Articles in reviewed journals

1. Rozenblatt, S., **Eizenberg, O.**, Ben-Levy, R., Lavie, V. and Bellini, W. J. (1985a).
Sequence Homology within the Morbilliviruses.
J. Virol. 53: 684-690.

2. Rozenblatt, S., **Eizenberg, O.**, Englund, G. and Bellini, W. J. (1985b). Cloning and Characterization of DNA Complementary to the Canine Distemper Virus mRNA Encoding Matrix, Phosphoprotein, and Nucleocapsid Protein.
10th. Virol. 53: 691-694.

3. **Eizenberg, O.**, and Oren, M. (1991).
Reduced Levels of α1 (I) Collagen mRNA in Cells Immortalized by Mutant p53 or Transformed by ras.
Biochemica et Biophysica Acta 1129: 34-42.

4. **Eizenberg, O.**, Kaplitt, M.G., Eitan, S., Pfaff, D.W., Hirschberg, D.L. and Schwartz, M. (1994).
Linear Dimeric Interleukin-2 Obtained by the Use of a Defective Herpes Simplex Viral Vector: Conformation-Activity Relationship.
Mol. Brain Research 2: 156-162.

5. **Eizenberg, O.**, Faber-Elman, A., Lotan, M. and Schwartz, M. (1995a). Interleukin-2 Transcripts in Human and Rodent Brains: Possible Expression by Asrocytes.
J. Neurochemistry 64: 1928-1936.

6. **Eizenberg, O.**, Faber-Elman, A., Gottlieb, E., Oren, M., Rotter, V. and Schwartz, M. (1995b).
Direct Involvement of p53 in Programmed Cell Death of Oligodendrocytes.
EMBO J. 14 (6): 1136-1144.

7. **Eizenberg, O.**, Gottlieb, E., Faber-Elman, A., Oren, M., Rotter, V. and Schwartz, M. (1996).
p53, a key regulatory protein in central nervous system differentiation and apoptosis.
Mol. Cell. Biol. 16 (9): 5178-5185.

8. Monsonego, A., Shani, Y., Friedmann, I., Paas, Y., **Eizenberg, O.** and Schwartz, M. (1997).
Expression of GTP-dependent and GTP-independent tissue-type transglutaminase in cytokine-treated rat brain astrocytes.
10th. Biol. Chem. 272: 3724-3732.

9. Fisher, A., Brandis, R., Haring, R., Eshhar, N., Heldman, E., Karton, Y., **Eizenberg, O.**, Meshulam, H., Marciano, D. and Pittel, Z. (1998).
Novel m1 muscarinic agonists in treatment and delaying the progression of Alzheimer's disease - an unifying hypothesis.
J. Physiol. (Paris) 92: 337-340.

10. **Eizenberg, O.**, Grabovsky, V., Vaizel- Ohayon, D., and Peled, A. (2006).
"Novel therapeutics for metastatic cancer – BKTRP3 and its derivatives".
(In preparation).

11. Gavish, M., Peled, A., **Eizenberg O.**, Vaizel-Ohayon, D., and Chor, B. (2006).
"Genetic Code Symmetry and an Efficient Algorithm foe Efficient Cloning".
(In preparation).

2. Articles of symposia proceedings

1a. Rozenblatt, S., Lavie, V., **Eizenberg, O.** (June, 1983).
Persistent Virus Infections in Slow Neurobiological Diseases.
Nucle(ol)ar Workshop BANYHOS-Sur-Mer, France.

3. Abstracts

1. **Eizenberg, O.**, Faber-Elman, A., and Schwartz, M. (October, 1993). Detection of Interleukin-2 Transcripts in Human and Rodent Brains; Astrocytes as a possible source for brain IL-2.
The second Stanford International Neuroscience Symposium: Gene Expression in the Central Nervous System, China.

2. **Eizenberg, O.**, Faber-Elman, A., Lotan, M. and Schwartz, M. (December, 1993).
Interleukin-2 Transcripts in Mammalian Brain: Possible Expression of Brain Originated IL-2 by Astrocytes.
The Second Israeli Neuroscience Conference, Israel.

3. **Eizenberg, O.**, Faber-Elman, A. and Schwartz, M. (March, 1994)
Dimeric IL-2 Induces Apoptotic Cell Death of Oligodendrocytes.
The Annual Meeting of the Israeli Committee for Biochemistry and Molecular Biology, Israel.

4. **Eizenberg, O.**, Faber-Elman, A., Gottlieb, E., Oren, M., Rotter, V., Lavie, V. and Schwartz, M. (November, 1994).
Direct Involvement of p53 in programmed cell death of oligodendrocytes.
Society for Neuroscience, 24th annual meeting, Miami Beach, Florida, USA.

5. **Eizenberg, O.**, Gottlieb, E., Oren, M., Rotter, V. and Schwartz, M. (December, 1994).
p53, a key regulatory protein in the nervous system.
Israel Society for Neuroscience, 3rd annual meeting, Eilat, Israel.

6. **Eizenberg, O.**, Gottlieb, E., Faber-Elman, A., Oren, M., Rotter, V. and Schwartz, M. (November, 1995).
Direct Involvement of p53 in central nervous system differentiation and apoptosis.
Federation of the Israel Societies of Experimental Biology (F.I.S.E.B.), first meeting, Eilat, Israel.

7. **Eizenberg, O.**, Gottlieb, E., Faber-Elman, A., Oren, M., Rotter, V. and Schwartz, M. (November 1995).
The regulatory proteins p53 and Bax Involvement in neuronal and oligodendrocyte cell cycle regulation.
Society for Neuroscience, 25th annual meeting, San Diego, California, USA.

8. **Eizenberg, O.**, Faber-Elman, A., Gottlieb, E., Oren, M., Rotter, V. and Schwartz, M. (December, 1995).
Central Nervous system differentiation and apoptosis: direct involvement of p53 and possibly of Bax.
Israel Society for Neuroscience, 4th annual meeting, Eilat, Israel.

9. Fisher, A., Haring, R., Pittel, Z., Brandis, R., Eshhar, N., Karton, Y., Meshulam, H., **Eizenberg, O.**, Marciano, D. and Heldman, E. (April, 1998).
M1 muscarinic agonists from treatment to delaying the progression of Alzheimer's Disease (AD).
Fifth Int. Geneva/Springfield Symposium on advances in Alzheimer Therapy, Geneva, Switzerland.

10. Fisher, A., Haring, R., Pittel, Z., Heldman, E., Brandis, R., Eshhar, N., Meshulam, H., **Eizenberg, O.**, Marciano, D. and Karton, Y. (July, 1998).
M1 muscarinic agonists in treatment and delaying the progression of Alzheimer's disease (AD) - An unifying hypothesis.
The 6th International Conference on Alzheimer's Disease and related Disorders, Amsterdam, Netherlands.

11. Fisher, A., Haring, R., Pittel, Z., Heldman, E., Brandis, R., Eshhar, N., Meshulam, H., **Eizenberg, O.**, Marciano, D. and Karton Y. (October, 1998).
M1 selective muscarinic agonists: from treatment toward delaying the progression of Alzheimer's disease.
4th Hungarian Conference on Alzheimer's Disease and Related disorders, Szeged, Hungary.

12. Fisher, A., Haring, R., Pittel, Z., Heldman, E., Brandeis, R., **Eizenberg, O.**, Esshar, N., Mesulam, H., Bar-Ner, N., Marcovitch, I. And Karton, Y. (November 1998).
M1 Muscarinic Agonist – New Prospects in the Therapy of Alzheimer's Disease.
International Workshop on Conformational Diseases, Ein-Boqeq, Dead Sea, Israel.

13. Haring, R., **Eizenberg, O.**, Pittel, Z. and Fisher, A. (July 2000).
M1 Muscarinic Agonists Protect PC12M1 Cells from Growth Factor Deprivation and β-Amyloids-induced Apoptosis.
World Alzheimer Congress 2000, Neurobiology of Aging, Washington, D.C., U.S.A.

14. **Eizenberg, O.**, Ezerzer, C., Vaizel, D., Grabovsky, V. and Pele, A. (March 2003).
"Identification of chemokine-binding peptides with an antagonist and agonist bioactivity."
"Chemokines in Immunity", 6th Winter Conference in Immunology, St. Sorlin d'Arves Workshop, Alpes, France.

15. **Eizenberg, O.**, Ezerzer, C., Vaizel, D., Grabovsky, V. and Peled, A. (May, 2003).
"Development of a novel platform technology for the identification of chemokine binding peptides with agonistic and antagonistic properties.
2nd Bio-Tech Israel 2003 Conference, Tel – Aviv, Israe.

16. **Eizenberg, O.**, Grabovsky, V., Vaizel- Ohayon, D., Ezerzer, C., and Peled, A. (May, 2004).
"Development of Novel Therapeutics to Target Cancer and Inflamation".
3rd Bio-Tech Israel 2004 Conference, Tel – Aviv, Israel.

17. **Eizenberg, O.**, Grabovsky, V., Vaizel- Ohayon, D., and Peled, A. (November, 2005).
"Development of Novel Anti-Chemokine Therapeutics".
1st INNOCHEM meeting, Milan, Italy.

18. **Eizenberg, O.**, Grabovsky, V., Vaizel- Ohayon, D., Eizenberg, I. and Peled, A. (October 2006).
"Novel Chemokine Binding Peptides Capable of Modulating the Biological Activity of Chemokines".
2nd INNOCHEM meeting, Belinzona, Suizerland.

19. **Eizenberg, O.**, Grabovsky, V., Vaizel- Ohayon, D., Eizenberg, I. and Peled, A. (December 2006).
"Development of novel anti-chemokine therapeutics".
1st MYASTAID meeting, Paris, France.

4. Patents

1. Peled, A., **Eizenberg, O.** and Vaizel-Ohayon, D. (July, 2005).
US Patent: "Novel Method for Screening for Chemokine/Cytokine Antagonists and Agonists".

2. Peled, A., Ezerzer, C., Vaizel-Ohayon, D. and **Eizenberg, O.** (November, 2005).
US Patent: Novel Method for Screening for Modulators of GPCR Activity".

3. Peled, A., Ezerzer, C., Vaizel-Ohayon, D. and **Eizenberg, O.** (August, 2005). US Patent: "Chemokine Binding Site and Novel Chemokine Antagonists and Agonists Derived Therefrom".

4. Peled, A., **Eizenberg, O.** and Vaizel-Ohayon, D. (February, 2002). US Patent: Novel Chemokine Binding Peptides Capable of Modulating the Biological Activity of Chemokines".

5. Peled, A., **Eizenberg, O.** and Vaizel-Ohayon, D. (February, 2002). European Patent: Novel Chemokine Binding Peptides Capable of Modulating the Biological Activity of Chemokines".